

thereof, said second DNA segment comprises an *attP* sequence according to SEQ ID NO:2 or a derivative thereof, wherein if said first DNA segment comprises an *attP* sequence according to SEQ ID NO:2 or a derivative thereof, said second DNA segment comprises an *attB* sequence according to SEQ ID NO:1 or a derivative thereof, wherein if said first DNA segment comprises an *attL* sequence according to SEQ ID NO:3 or a derivative thereof said second DNA segment comprises an *attR* sequence according to SEQ ID NO:4 or a derivative thereof, or wherein if said first DNA segment comprises an *attR* sequence according to SEQ ID NO:4 or a derivative thereof said second DNA segment comprises an *attL* sequence according to SEQ ID NO:3 or a derivative thereof; and

wherein said cell further expresses a bacteriophage *lambda* integrase Int, which induces sequence specific recombination through said *attB* and *attP* or *attR* and *attL* sequences.

30. (New) The method of claim 29, wherein said first DNA segment was introduced into the genome of said cell by recombinant methods.
31. (New) The method of claim 29, wherein said first DNA segment is naturally-occurring in the genome of said cell.
32. (New) The method of claim 29, wherein said first DNA segment comprises an *attB* sequence according to SEQ ID NO:1 or a derivative thereof, and said second DNA comprises an *attP* sequence according to SEQ ID NO:2 or a derivative thereof.
33. (New) The method of claim 29, wherein said first DNA segment comprises an *attP* sequence according to SEQ ID NO:2 or a derivative thereof, and said second DNA comprises an *attB* sequence according to SEQ ID NO:1 or a derivative thereof.
34. (New) The method of claim 29, wherein said first DNA segment comprises an *attL* sequence according to SEQ ID NO:3 or a derivative thereof, and said second DNA sequence comprises an *attR* sequence according to SEQ ID NO:4 or a derivative thereof, further comprising, in step (c), providing to said cell a Xis factor.

A2  
CONT.

- 35. (New) The method of claim 29, wherein said first DNA segment comprises an *attR* sequence according to SEQ ID NO:4 or a derivative thereof, and said second DNA sequence comprises an *attL* sequence according to SEQ ID NO:3 or a derivative thereof, further comprising, in step (c), providing to said cell a *Xis* factor.
- 36. (New) The method of claim 29, further comprising providing to said cell a third DNA segment comprising an *Int* gene. ((Steve, the third segment should only be the *Int* gene, the fourth segment should be the *Xis* factor gene. The *Int* is essential for the recombination of all four *att*-sites, the *Xis* factor gene only for the reaction between *attR* and *attL*.)
- 37. (New) The method of claim 36, further comprising providing to said cell a fourth DNA segment comprising *Xis* factor gene, respectively.
- 38. (New) The method of claim 36, wherein said third DNA segment further comprises a regulatory sequence effecting a spatial and/or temporal expression of the *Int* gene. ((Steve, please take care that all possibilities of original claim 6 are claimed))
- 39. (New) The method of claim 37, wherein said fourth DNA segment further comprises a regulatory sequence effecting a spatial and/or temporal expression of the *Xis* factor gene.
- 40. (New) The method of claim 29 wherein said *Int* is a modified integrase.
- 41. (New) The method of claim 37, wherein said modified *Int* is *Int-h* or *Int-h/218*.
- 42. (New) The method according to claim 29, wherein in step (c) further comprises providing an "integration host factor" (IHF).
- 43. (New) The method according to claim 29, wherein said first and/or second DNA segment further comprise a sequence effecting integration of said first and/or second DNA segment into the genome of said cell by homologous recombination.
- 44. (New) The method of claim 29, wherein said first and/or second DNA segment further comprises a sequence coding for a polypeptide of interest.

A2  
CONT.

- 45. (New) The method of claim 44, wherein said polypeptide of interest is a structural protein, an endogenous or exogenous enzyme, a regulatory protein or a marker protein.
- 46. (New) The method of claim 29, wherein said first and second DNA segment are introduced into the eukaryotic cell on the same DNA molecule.
- 47. (New) The method of claim 29, wherein said eukaryotic cell is a mammalian cell.
- 48. (New) The method of claim 47, wherein said mammalian cell is a human, simian, mouse, rat, rabbit, hamster, goat, bovine, sheep or pig cell.
- 49. (New) The method of claim 29, further comprising:
  - (d) performing a second sequence specific recombination of DNA by an Int and a Xis factor after the steps (a)-(c), wherein said first DNA sequence comprises said *attB* sequence according to SEQ ID NO:1 or a derivative thereof and said second DNA sequence comprises the *attP* sequence according to SEQ ID NO:2 or a derivative thereof, or wherein said first DNA sequence comprises said *attP* sequence according to SEQ ID NO:2 or a derivative thereof and said second DNA sequence comprises the *attB* sequence according to SEQ ID NO:1 or a derivative thereof.
- 50. (New) The method of claim 49, further introducing a further DNA sequence into said cells, the further DNA sequence comprising a Xis factor gene.
- 51. (New) The method of claim 50, wherein said further DNA sequence comprises further a regulatory DNA sequence effecting a spatial and/or temporal expression of said Xis factor gene.
- 52. (New) The method of claim 29, wherein said method is performed in a vertebrate organism.
- 53. (New) The method of claim 52, wherein said vertebrate organism is a human.

*Ad*  
*COOT.*

54. (New) A nucleic acid comprising the sequence of SEQ ID NO:5, or a derivative thereof having as many as six substitutions, with the provision that the derivative is not the wild-type *attP* sequence.
55. (New) A vector comprising:
  - (a) a nucleic acid segment comprising the sequence of SEQ ID NO:5, or a derivative thereof having as many as six substitutions, with the provision that the derivative is not the wild-type *attP* sequence; and
  - (b) a nucleic acid segment coding for a selected gene or a fragment thereof.
56. (New) The vector of claim 53, wherein said selected gene is the CFTR gene, ADA gene, LDL receptor gene,  $\beta$  globin gene, Factor VIII gene or Factor IX gene, alpha-1-antitrypsin gene or the dystropin gene or a gene fragment of one of said genes.
57. (New) The vector of 53, further comprising a nucleic acid segment comprising a regulatory element.
58. (New) A eukaryotic cell obtainable according to the method of claim 29.
59. (New) A non-human transgenic organism comprising at least one cell made according to the method of claim 29.
60. (New) The organism according to claim 54, wherein said organism is a mouse, rat rabbit or hamster.

---

#### REMARKS

Should the examiner have any questions regarding the content of this preliminary amendment, a telephone call to the undersigned is invited.